Remarks

The Office Action mailed June 13, 2001 has been received and reviewed. Claims 1-17 and 19-20 are pending in the application. These claims stand rejected. Claim 18 has been canceled without prejudice or disclaimer. The application is to be amended as previously set forth including the addition of claims 21-22. All amendments are made without prejudice or disclaimer. Reconsideration is respectfully requested.

1. Rejection of Claims 1-3, 7, and 18-20 Under 35 U.S.C. § 102(e) - Dellaporta

Claims 1-3, 7, and 18-20 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Dellaporta (U.S. Patent 6,013,486). Applicants have amended the claims and respectfully traverse the rejection.

"For anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly." M.P.E.P. § 706.02. Dellaporta discloses "hybridizing the array with a solution containing a marked (labeled) probe. For detection of a mutation in a specific gene, this will typically involve the use of a cloned DNA segment including that gene sequence used as a probe." U.S. Patent 6,013,486, col.15, ll. 13-14. Claim 1 has been amended to recite that the insertion element library is built in a 3D-array of block, row and column pools. Basis for the amendment is found in the last full paragraph of page 7 of the application as filed. Applicants would respectfully point out that Dellaporta is not believed to disclose an insertion element library built in a 3D-array of block, row and column pools. Accordingly, the rejection of claim 1 as being anticipated should be withdrawn.

Likewise, Dellaporta is not believed to disclose the particular method of amended claim 19 in all of its features, and the applicants thus respectfully request that the 102(e) rejection of claim 19 be withdrawn.

2. Rejection of Claim 4 Under 35 U.S.C. § 103(a) - Dellaporta & Souer et al.

Claim 4 stands rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Dellaporta and Souer et al. Applicants respectfully traverse the rejection of claim 4 on the basis that no prima facie case of obviousness has been set forth.

When an independent claim is not obvious, then any claim depending from the dependent

claim is also not obvious. M.P.E.P. §2143.03 (citing *In re Fine*, 5 USPQ2d 1596). Therefore, dependent claim 4 is allowable, at the very least, as depending directly or indirectly from inventive independent claim 1.

M.P.E.P. § 706.02(j) sets forth the standard for a Section 103(a) rejection:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). (Emphasis added).

M.P.E.P. § 2142 states:

> To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. *Ex parte Clapp*, 227 USPQ 972, 972 (Bd. Pat. App. & Inter. 1985). (Emphasis added).

Applicants respectfully submit that the Dellaporta and Souer et al. references do not expressly or implicitly suggest claim 4. Applicants also respectfully submit that the examiner has not presented a line of reasoning as to why the claimed invention would be obvious. The examiner indicated that the use of the re-amplification step in Sour et al. would have been obvious to those of ordinary skilled in the art in the method of Dellaporta. (Office Action, p. 4, lines 5-7).

The re-amplification step of Souer et at. would not have been obvious to use in the method of Dellaporta and that no motivation exists to combine the references as indicated in the Office Action.

"The examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998). The Office Action asserts that the motivation to combine the references would have been that the re-amplification step of Sour et al. would improve the yield of

the amplification reaction. (Office Action, p. 4, lines 7-8). M.P.E.P. 2143.01 states "the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). The applicants respectfully suggest that no motivation exists to combine the references as suggested in the Office Action.

The applicants respectfully submit that when the references and the present claims are viewed as a whole, the claimed invention would not be obvious in view of the Dellaporta and Souer et al. references. M.P.E.P. § 2141.02 states:

> Ascertaining the differences between the prior art and the claims at issue requires interpreting the claim language, and considering both the invention and the prior art references as a whole... In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983). (Emphasis in original).

The Office Action asserts that the applicants' re-amplification step would be obvious to one skilled in the art based on the re-amplification step of Souer et al. combined with Dellaporta. However, when the prior art methods are viewed as a whole, Dellaporta teaches away from Sour et al. because Dellaporta discloses a method for isolating gene insertion mutants, while Souer et al. discloses a method of isolating genes tagged by a transposable element. The goals are opposite. Souer et al. discloses a method using forward genetics, where mutants have been isolated and the researcher is looking for the mutated gene. In contrast, Dellaporta discloses a method of reverse genetics, where a population is screened for an insertion event in a specific gene.

"It is improper to combine references where the references teach away from their combination." *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). M.P.E.P. § 2145. The Dellaporta patent and the Souer et al. reference considered in their entirety cannot be used or combined to render claim 4 obvious because the Dellaporta patent teaches away from the Souer et al. reference.

3. Rejection of claims 5, 6, 8 and 12 Under 35 U.S.C. § 103(a) - Dellaporta & Vos et al.

Claims 5, 6, 8 and 12 stand rejected under 35 U.S.C. § 103(a) as being obvious over Dellaporta as applied to claim 1, and further in view of Vos et al. Applicants respectfully traverse

the rejection, as hereinafter set forth.

Applicants' have amended claim 1 to include the limitations include the feature that the insertion element library is built in a 3D-array of block, row and column pools. When an independent claim is not obvious, then any claim depending from the dependent claim is also not obvious. M.P.E.P. §2143.03 (citing *In re Fine*, 5 USPQ2d 1596). Therefore, dependent claims 5, 6, 8 and 12 are allowable, at the very least, as depending directly or indirectly from inventive independent claim 1.

Applicants further submit that the Office has not set forth a prima facie case of obviousness with respect to claims 5, 6, 8 and 12. Vos et al. is being improperly combined with Dellaporta because Vos et al. teaches away from the Dellaporta patent. The Office Action asserts that "it would have been obvious . . . to have used the DNA amplification method of Vos et al. with the library of gene insertion mutants of Dellaporta with a reasonable expectation of success." (Office Action, p. 5, lines 17-19). Vos et al. teaches a method of DNA fingerprinting, where the DNA of interest is characterized by the "fingerprint" produced when the amplified DNA is run on a gel. Vos et al. does not disclose a method of screening for an individual mutant as disclosed in Dellaporta, but rather discloses a method of mapping the genome of an individual mutant. Because Vos et al. teaches away from Dellaporta and would not have been readily combinable, it would not have been obvious to one skilled in the art to amplify the library of gene insertion mutants in Dellaporta with the re-amplification method in Vos et al.

"It is improper to combine references where the references teach away from their combination." *In re Grasselli*, 713 F.2d at 743, 218 USPQ at 779; M.P.E.P. § 2145. Because Vos et al. teaches away from Dellaporta, the 103(a) rejection of claims 5, 6, 8 and 12 is improper and should be withdrawn.

Applicants further disagree with the contention that Vos et al. teaches transposon display amplification. (Office Action, p. 5, line 5). In fact, Vos et al. does not use transposon display, but rather teaches a technique for DNA fingerprinting known as "AFLP". The difference between the two techniques is that the primers used in transposon display are based on the insertion element sequence and are specific for a known sequence within the insertion element sequence, while the sequence of the AFLP primers are random, and can be based on any sequence used to create the adapter.

Since Vos et al. does not in fact disclose transposon display, a convincing line of reasoning of why the references should be combined or what combination results has not been provided, and the Section 103(a) rejection of claims 5, 6, 8 and 12 is improper and should be withdrawn.

4. Rejection of Claims 9 and 10 Under 35 U.S.C. § 103(a) - Dellaporta & Koes et al.

Claims 9 and 10 stand rejected under 35 U.S.C. § 103(a) as being obvious over Dellaporta as applied to claim 1, in view of Koes et al. Applicants respectfully traverse the rejection, as hereinafter set forth. When an independent claim is not obvious, then any claim depending from the dependent claim is also not obvious. M.P.E.P. §2143.03 (citing *In re Fine*, 5 USPQ2d 1596). Therefore, dependent claims 9 and 10 are allowable, at the very least, as depending directly or indirectly from inventive independent claim 1.

5. Rejection of Claims 13-17 Under 35 U.S.C. § 103(a) - Dellaporta

Claims 13-17 stand rejected under 35 U.S.C. § 103(a) as being obvious over Dellaporta as applied to claim 1. Applicants respectfully traverse the rejection, as hereinafter set forth. When an independent claim is not obvious, then any claim depending from the dependent claim is also not obvious. Id. Therefore, dependent claims 13-17 are allowable, for among other things, as depending directly or indirectly from not obvious independent claim 1.

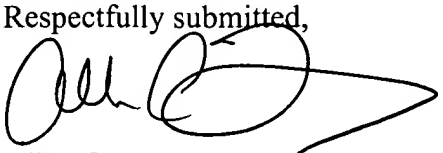
6. Rejection of Claim 11 in the Office Action Summary

Claim 11 stands rejected in the Office Action Summary, but was not discussed in the Detailed Action. As previously stated, when an independent claim is not obvious, then any claim depending from the dependent claim is also not obvious. Id. Therefore, dependent claim 11 is allowable, *inter alia*, as depending directly from not obvious independent claim 3.

Conclusion

In view of the amendments and remarks presented herein, applicants respectfully submit that claims 1-17 and 19-22 are allowable, and an early notice thereof is respectfully solicited. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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Attachment: Marked up version of the amended claims

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Thrice amended) A method for simultaneous screening for one or more gene insertion mutants in a population of any organism comprising:

preparing an insertion element mutant library comprising a plurality of nucleic acid insertion elements and insertion element flanking sequences, said insertion element flanking sequences originating from a defined population of an organism wherein said gene insertion mutants are to be detected and wherein said insertion element library is built in a 3D-array of block, row and column pools;

amplifying said insertion element flanking sequences from said [insertion element mutant library] block, row and column pools using at least one primer derived from a sequence of a nucleic acid insertion element of said plurality of nucleic acid insertion elements; and

fixing a set of nucleic acid amplification products representing said insertion element flanking sequences derived from said [insertion element mutant library] block, row and column pools to a solid support as target for hybridization.

2. (Thrice amended) The method according to claim 1 wherein the set of nucleic acid amplification products representing said [insertion] element flanking sequences representing said block, row and column pools are obtained by iPCR using at least one primer or a set of primers based on a sequence of at least one nucleic acid insertion element.

3. (Twice Amended) The method according to claim 2 wherein said iPCR comprises:

digesting nucleic acid sequences of said [insertion element mutant library] block, row and column pools with at least one restriction enzyme resulting in a collection of amplifyable genomic fragments;

ligating at least one amplifyable genomic fragment by self ligation; and

amplifying said at least one amplifyable genomic fragment using a set of internal primers.

5. (Twice Amended) The method according to claim 1 wherein amplifying insertion element flanking sequences from said insertion element mutant library built in the 3D-array of block, row and column pools comprises amplifying said insertion element flanking sequences using transposon display amplification.

19. (Twice Amended) A method for simultaneous screening for one or more gene insertion mutants in a population of any organism comprising:

preparing an insertion element mutant library comprising a plurality of nucleic acid insertion elements and insertion element flanking sequences, said insertion element flanking sequences originating from a defined population of an organism wherein said gene insertion mutants are to be detected and wherein said insertion element library is built in a 3D-array of block, row and column pools;

amplifying said insertion element flanking sequences from said insertion element mutant library using at least one primer derived from a sequence of a nucleic acid insertion element of said plurality of nucleic acid insertion elements; and

producing a set of labelled amplification products representing said insertion element flanking sequences derived from said [insertion element mutant library] block, row and column pools to use as probes to hybridize to a solid support to which one or more nucleic acids have been fixed as target(s) for hybridisation.